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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,879	07/29/2003	Cherng-Ju Kim	14498	7934

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EXAMINER	
SASAN, ARADHANA	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,879	KIM, CHERNG-JU	
	Examiner	Art Unit	
	Aradhana Sasan	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-16,18-23,25-37 and 39-41* is/are pending in the application.

4a) Of the above claim(s) *15,16,18,36,37 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-14, 19-23, 25-35, 40-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 08/07/2007 are acknowledged.

2. Claims 7 and 24 were cancelled.

3. Claims 15-16, 18, 36-37, and 39 were withdrawn.

4. Claims 1, 19 and 40 were amended.

5. Claims 1-6, 8-14, 19-23, 25-35, 40-41 are included in the prosecution.

Response to Arguments

Rejection of claims 1-14, 19-35, and 40-41 under 35 USC § 103(a)

6. Applicant's arguments, see Page 10, filed 08/07/2007, with respect to the rejection of claims 1-14, 19-35, and 40-41 under 35 USC § 103(a) as being unpatentable over Kim (US 6,110,500) in view of Marvola et al. (US 5,962,024) have been fully considered but are not persuasive.

Applicant argues that all of the independent claims 1, 19, and 40 are limited to a perforated tablet, "wherein the drug is released from the perforated tablet at a zero-order, or near zero-order kinetic release rate, in the aqueous environment above a pH of about 5" and that Kim does not teach this limitation. This is not persuasive because Kim teaches a tablet that "achieves nearly linear (zero-order), or parabolic release kinetics for delivering water-soluble drugs over a long period of time at a nearly constant rate" (Col. 2, lines 47-51). The combination of a tablet with controlled release of an active ingredient and "nearly linear (zero-order)" release kinetics (as taught by Kim) with the teaching of a pH sensitive enteric polymer coating (which is known in the art to allow

the release of active ingredients in an environment with a pH above 5) as taught by Marvola, would have lead one with ordinary skill in the art at the time the invention was made to arrive at the instant invention.

Applicant argues that there is no suggestion in Marvola that the combination of the pH sensitive polymer, when formed into a perforated tablet, would exhibit zero-order kinetics. This is not found persuasive because the primary reference, Kim, teaches nearly linear (zero-order) release kinetics for a tablet that has a hydrophobic coating over the core (Col. 1, lines 64-67). Enteric polymers are known in the art to be hydrophobic. Marvola teaches pH sensitive enteric polymers which are hydrophobic. Therefore, one skilled in the art would find the claimed elements in Kim (near zero order release kinetics, perforated tablet, and hydrophobic polymer) and Marvola (enteric polymer coating). The motivation to combine the references is provided by the Marvola teaching that the pH sensitive enteric polymer dissolves only in the upper part of the colon (Col. 2, lines 33-36). One skilled in the art could have combined the elements and the combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. - , 82 USPQ2d 1385 (2007).

Applicant argues that Kim does not provide this motivation and that there is no teaching that varying the amount of (enteric) polymer, either in Kim or Marvola, would change the kinetic release rate of the drug. However, Marvola teaches: "... a peroral composition providing controlled release of a drug, the composition comprising a) a core comprising the drug and drug release controlling agent and b) an enteric coating, in which composition the drug release controlling agent substantially consists of a pH-

sensitive enteric polymer" (Col. 1, lines 56-61). Therefore, one skilled in the art would know that by modifying the "drug release controlling agent" or the "pH-sensitive enteric polymer" the drug release rate could be modified. Therefore, modification of the kinetic release rate of the drug is taught by Marvola.

Applicant argues that the examiner has not shown a motivation to combine the references. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). As mentioned above, one skilled in the art would find the claimed elements in Kim (near zero order release kinetics, perforated tablet, and hydrophobic polymer) and Marvola (enteric polymer coating as the drug release controlling agent). One skilled in the art could have combined the elements and the combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. -, 82 USPQ2d 1385 (2007).

Therefore, the rejection of 5/30/07 is maintained.

MAINTAINED REJECTIONS:

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-14, 19-35, 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim (US 6,110,500 in view of Marvola et al. (US 5,962,024).

The claimed invention is a perforated tablet for the controlled release of a drug comprising a mixture of an enteric polymer and a drug (the enteric polymer is substantially hydrophobic and substantially soluble in a substantially aqueous environment above a pH of about 5).

Kim teaches a tablet for the controlled release of an active pharmaceutical ingredient (Abstract). "The tablet comprises a body having a donut-like configuration with a cylindrical hole extending coaxially through the center of the body. The core material of the body comprises at least one active pharmaceutical agent and at least one hydrophilic, water-soluble, polymeric carrier" (Col. 1, lines 59-64). The active pharmaceutical agent is blended with the hydrophilic, water-soluble polymeric carrier, and the "mix" is compressed into a tablet (Col. 2, lines 3-7). Kim also uses the term "perforated" to describe the tablets with a donut-like hole (Col. 7, lines 6-10).

Kim does not expressly teach a mixture of active pharmaceutical agent and an enteric polymer (which is substantially hydrophobic and substantially soluble in a substantially aqueous environment above a pH of about 5).

Marvola teaches a peroral composition for the controlled release of a drug (Abstract). The composition comprises "a) a core comprising the drug and a drug release controlling agent and b) an enteric coating, in which composition the drug release controlling agent substantially consists of a pH sensitive enteric polymer" (Col.

1, lines 56-61). Marvola teaches that "of the agent used in the core for controlling drug release, ... most preferably 100% consists of a pH sensitive enteric polymer" (Col. 2, lines 12-15). The drug is mixed with a filler, and granulated with "an aqueous or ethanol solution of a suitable enteric polymer" (Col. 2, line 66 to Col. 3, line 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the tablet with a donut-like hole through the center of the body for controlled release of a drug ("perforated") and with a core containing a mixture of a drug and a polymeric carrier, as suggested by Kim, and combine it with the composition comprising a mixture of a drug and a drug release controlling agent (pH sensitive enteric polymer), as suggested by Marvola, and produce the instant invention.

One of ordinary skill in the art would have been motivated to this because incorporating the pH sensitive enteric polymer with the drug in the tablet matrix allows protection of the drug from the gastric acids and release in the intestine where the pH is above about 5. Marvola teaches "a pH sensitive enteric polymer, the dissolving of which must not begin until the lower part of the small intestine or in the upper part of the colon" (Col. 2, lines 33-36).

Regarding instant claim 1, one with ordinary skill in the art would find it obvious to make the perforated tablet with a core containing a mixture of a drug and a polymeric carrier, as suggested by Kim, and combine it with the composition comprising a mixture of a drug and a drug release controlling agent (pH sensitive enteric polymer), as suggested by Marvola, and produce the instant invention. The limitation of the enteric polymer of instant claim 1 being substantially soluble in a substantially aqueous

environment above a pH of about 5 would be obvious to one with ordinary skill in the art given the Marvola disclosure of "the pH dissolution point of the pH-sensitive enteric polymer in the core must be higher than 6.0 ..." (Col. 2, lines 17-19).

Regarding the limitation of plurality of layers of the perforated tablet of instant claim 2, and the inner and outer layered perforated tablet of instant claim 19, one with ordinary skill in the art would find it obvious to formulate a layered perforated tablet with a mixture of drug and enteric polymer as taught by Kim and Marvola in order to optimize the controlled release profile of the drug. One with ordinary skill in the tableting art would find it obvious to prepare tablets with layers of the drug and polymer mixture and prepare the tablets with this drug and polymer mixture layer as the inner layer in order to protect the drug. The polymer can be a hydrophilic polymer (substantially water soluble), as taught by Kim, or an enteric polymer, as taught by Marvola.

The limitation of the cylindrically shaped tablet with the perforation extending through the center of the tablet of instant claims 3 and 20 would have been obvious to one with ordinary skill in the tableting art over the teaching by Kim of a tablet "with a cylindrical hole extending coaxially through the center of the body" (Col. 1, lines 59-61).

The limitation of the enteric polymer of instant claims 4-6 and 21-23 would have been obvious to one with ordinary skill in the art over the Marvola teaching of pH sensitive enteric polymers hydroxypropylmethyl cellulose acetate succinate and methacrylic acid methylmethacrylate copolymer (Col. 2, lines 20-24).

The enteric polymer present in amount to control the release of the drug at a substantially linear rate over time of instant claim 7 and 24 would have been obvious to

one with ordinary skill in the art over the "nearly linear (zero order)" release profile attained by the tablet taught by Kim (Col. 2, lines 48-51). One skilled in the art would vary the amount of the enteric polymer in the formulation in order to achieve the linear release rate for the drug during the process of routine experimentation.

The ranges of the enteric polymer of instant claims 8-10 and 25-27 would have been obvious to one with ordinary skill in the art over the Marvola teaching that: "the amount of the drug release controlling agent is about 0.1-20%, preferably 2-10%, of the weight of the core" (Col. 2, lines 53-54). One with ordinary skill in the art would vary the amount of the enteric polymer in the tablet formulation in order to achieve the desired linear release profile for the drug.

Regarding instant claims 11-12, 28-29, the binder would have been obvious to one with ordinary skill in the art over the materials (HPMC, polyethylene dioxide and polyethylene glycol) used by Kim (Col. 4, Table of materials used).

The limitation of the binders of instant claims 13-14 and 30-31 would have been obvious to one with ordinary skill in the art over the Marvola teaching of methacrylic acid methylmethacrylate copolymer (Col. 2, lines 20-24).

The limitation of the outer layer water-insoluble components of instant claims 32-34 would have been obvious to one with ordinary skill in the art over the Marvola teaching of water insoluble polymers cellulose acetate phthalate, and methacrylic acid methylmethacrylate copolymer (Col. 2, lines 20-24).

The limitation of the outer layer water-soluble components of instant claim 35 would have been obvious to one with ordinary skill in the art over the polyethylene dioxide used by Kim (Col. 4, Table of materials used).

Regarding the product by process claims 40 and 41, the limitations of the perforated tablet for the controlled release of a drug, comprising a mixture of an enteric polymer and the drug, and the outer and inner layers of the tablet, would have been obvious to one of ordinary skill in the art over the perforated tablet with a core containing a mixture of a drug and a polymeric carrier, as suggested by Kim, and combining it with the composition comprising a mixture of a drug and a drug release controlling agent (pH sensitive enteric polymer), as taught by Marvola.

Conclusion

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MPW

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